Obstetric Medicine

Obstetric Medicine
2023, Vol. 16(4) 245–246

DOI: 10.1177/1753495X221113489
journals.sagepub.com/home/obm

Sage

Severe hyponatraemia peripartum associated with omeprazole therapy

Adam Morton[1,2]

Abstract

Hyponatraemia is the most commonly encountered electrolyte abnormality in pregnancy and may be associated with adverse maternal and neonatal outcomes. Rapid onset, severe hyponatraemia has been reported with proton-pump inhibitor therapy in non-pregnant individuals. Gastro-oesophageal reflux is very common during pregnancy, and proton-pump inhibitors are available without a prescription in many countries. A case of severe maternal hyponatraemia in the setting of recent omeprazole therapy is presented. Health professionals should be aware of this complication given the availability of proton-pump inhibitors without prescription and high rates of gestational gastro-oesophageal reflux.

Keywords

Hyponatraemia, proton-pump inhibitor, omeprazole

Date Received: 10 December 2021; accepted: 22 June 2022

Introduction

In normal pregnancy, serum sodium (Na^+) falls by 3–5 mmol/L and average plasma osmolality by 5–10 mmol/L due to a reduction in osmotic threshold at which antidiuretic hormone (ADH) release and thirst stimulus occur.[1] Pregnancy outcomes in the setting of maternal hyponatraemia depend on both the rate of decline of serum Na + levels and absolute serum Na + concentration.[2] Clinical practice guidelines define mild hyponatraemia in non-pregnant individuals as serum Na + of 130–135 mmol/L, moderate 125–129 mmol/L, and severe less than 125 mmol/L as measured by an ion-specific electrode.[3] Values defining the severity of hyponatraemia in pregnancy have not been delineated taking into account the physiological change in serum Na +. Complications of hyponatraemia include headache, nausea, seizures and cerebral oedema. Equilibration of serum sodium across the placenta results in neonatal hyponatraemia, with potential complications of neonatal jaundice, tachypnoea, vomiting, weakness, seizures and increased risk of neonatal intensive care admission. Measurement of neonatal serum sodium is important particularly as seizures have been reported in the neonates of asymptomatic women with hyponatraemia.[4] A wide array of conditions is associated with hyponatraemia in pregnancy, hyperemesis gravidarum and preeclampsia the most common causes in the first and second half of pregnancy, respectively.[5] Treatment options for severe hyponatraemia due to syndrome of inappropriate antidiuretic hormone (SIADH) include fluid restriction, oral urea, hypertonic saline, oral salt tablets and vasopressin receptor antagonists. There is no safety data regarding the use of vasopressin receptor antagonists during pregnancy or breast feeding. Correction of maternal hyponatraemia must be undertaken judiciously given the risk of osmotic demyelination syndrome if serum Na + rises too rapidly.

Case report

A 41-year-old woman presented for a booked induction of labour at 38 weeks of gestation. Her past history was significant for laparoscopic sleeve gastrectomy 3 years earlier. The woman's preconception body mass index was 20.6 kg/m^2. Routine pathology tests were collected and dinoprostone was administered at 0820 h. Labour was established at 1500 h. The laboratory subsequently reported the woman's serum sodium had been 122 mmol/L (normal 130–145) on the pathology tests taken prior to induction. A review of previous results showed the woman's serum sodium had been 134 mmol/L at 20 weeks of gestation. Repeat serum sodium at 1540 h was 119 mmol/L. The woman was asymptomatic and proceeded to deliver a healthy female infant birthweight 2922 g at 1650 h. The woman denied excessive intake of fluids. She initially claimed no pharmacotherapy, however on specific questioning had been taking omeprazole 20 mg once daily for several days per week over the previous month for gastro-oesophageal reflux, the medication obtained over the counter without a prescription. She denied the use of herbal or complementary therapy. There were no symptoms or signs of pre-eclampsia, and the woman was clinically euvolaemic. Glucose, lipids, immunoglobulins, thyroid, adrenal and renal function were normal. Urine sodium and osmolality were 54 mmol/L and 218 mOsm/kg, respectively, and serum urate was 0.23 mmol/L (normal range 0.15–0.45), consistent with SIADH. A fluid restriction of 750 mL/day was initiated. The following morning serum sodium had risen to 131 mmol/L, improving further to 134 mmol/L on the second postpartum day. The woman's new-born had Apgar scores of 9 at 1 min and 10 at 5 min. The new born's serum sodium was 123 mmol/L and established breastfeeding within 2 h of delivery without signs of hyponatraemia.

[1]Obstetric Medicine, Mater Health, Raymond Terrace, South Brisbane, Australia
[2]University of Queensland, Herston, QLD, Australia

Corresponding author:
Adam Morton, Obstetric Medicine, Mater Health, Raymond Terrace, South Brisbane, 4101, Australia.
Email: adam.morton@mater.org.au

Discussion

A review of maternal hyponatraemia in a tertiary referral hospital over a 10-year period found the prevalence of serum Na + less than 130 mmol/L after 20 weeks of gestation to be 4.1 cases per 1000 deliveries.[6] Preeclampsia was the cause in 66.5% of cases other major causes including infection (13.4%), diabetes mellitus (3.1%) and acute fatty liver of pregnancy (2%). No cause was identified in 9.3% of cases. The prevalence of hyponatraemia in preeclampsia is 9–10%.[6] Additional causes of gestational hyponatraemia described in the literature include water intoxication during labour, prolonged labour, caesarean section, cortisol deficiency (due to Sheehan's syndrome, hypophysitis, Addison's disease) and medications (oxytocin, non-steroidal anti-inflammatory medications, thiazide diuretics).

A primary care database study found the point prevalence of prescription of proton-pump inhibitors (PPIs) in the United Kingdom was 7.7% in 2014.[7] Rates of PPI prescription during pregnancy are not known, although up to 80% of women are affected by gestational gastro-oesophageal reflux.[8] The possible association between pregnancy, hyponatraemia and PPI use has not been previously reported. PPI-associated hyponatraemia can be rapid-onset after commencing medication and may be associated with severe hyponatraemia with rapid recovery after cessation of therapy. Most cases occurred within 11 days of commencing therapy. One case report described a fall in serum sodium from 138 mmol/L (prior to therapy) to 117 mmol/L over a 36 h period.[9] The clinical and biochemical findings in case reports are consistent with SIADH as the mechanism of hyponatraemia. A population-based case-control study found adjusted odds ratios for hospitalisation due to hyponatraemia for newly initiated PPIs were omeprazole 2.67, pantoprazole 2.06, esomeprazole 2.89 and any PPI 2.78.[10] Two other studies found odds ratios indicating the association between PPI use and elderly patients with severe (OR 2.6) and moderate hyponatraemia (OR 4.4).[11,12] A study of 97 children and adolescents showed a significant increase in the frequency of decreased serum sodium following initiation of omeprazole therapy, with 17.5% developing serum sodium less than 135 mmol/L.[13]

In conclusion, proton-pump inhibitor therapy may be associated with the rapid onset of severe hyponatraemia. Health professionals involved in the care of pregnant women should be aware of this side-effect, particularly given the availability of PPIs without prescription.

Declaration of conflicting interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval exemption by Mater Health Human Research and Ethics Committee.

Funding

The author received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Adam Morton https://orcid.org/0000-0001-9887-714X

References

1. Cheung KL and Lafayette RA. Renal physiology of pregnancy. *Adv Chronic Kidney Dis* 2013; 20: 209–214.
2. Sterns RH. Disorders of plasma sodium. *N Engl J Med* 2015; 372: 1267–1269.
3. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Eur J Endocrinol* 2014; 170: G1–47.
4. Valerio E, Fantinato M, Giovannini IA, et al. Severe asymptomatic maternal antepartum hyponatremia leading to neonatal seizures: prevention is better than cure. *Matern Health Neonatol Perinatol* 2015; 1: 25.
5. Kabir S, Basher MS, Akhter H, et al. Clinico-biochemical profile of women with hyperemesis gravidarum admitted in a tertiary hospital. *Mymensingh Med J* 2017; 26: 483–489.
6. Morton A, Lumchee M, Kumar S, et al. Pregnancy outcomes in women with hyponatraemia and preeclampsia: case series and literature review. *Pregnancy Hypertens* 2021; 26: 38–41.
7. Othman F, Card TR and Crooks CJ. Proton pump inhibitor prescribing patterns in the UK: a primary care database study. *Pharmacoepidemiol Drug Saf* 2016; 25: 1079–1087.
8. Thelin CS and Richter JE. Review article: the management of heartburn during pregnancy and lactation. *Aliment Pharmacol Ther* 2020; 51: 421–434.
9. Morton A and Mackintosh J. Severe hyponatraemia associated with omeprazole. *Aust Prescr* 2005; 28: 48–49.
10. Falhammar H, Lindh JD, Calissendorff J, et al. Associations of proton pump inhibitors and hospitalization due to hyponatremia: a population-based case-control study. *Eur J Intern Med* 2019; 59: 65–69.
11. Correia L, Ferreira R, Correia I, et al. Severe hyponatremia in older patients at admission in an internal medicine department. *Arch Gerontol Geriatr* 2014; 59: 642–647.
12. Buon M, Gaillard C, Martin J, et al. Risk of proton pump inhibitor-induced mild hyponatremia in older adults. *J Am Geriatr Soc* 2013; 61: 2052–2054.
13. Famouri F, Derakhshani F, Madihi Y, et al. Electrolyte disturbances in children receiving omeprazole for gastroesophageal reflux disease. *J Res Med Sci* 2020; 25: 06.